

AMENDMENTS TO THE CLAIMS

The following claim listing is meant to replace all previous claim listings.

1. (Withdrawn) A method for the design and/or the selection of chemokines variants having agonist or antagonist property towards a ligand of GPCR of animal cells comprising the following steps:
 - A) obtaining a phage displayed library expressing on their surface said chemokine variants mutated within the domain responsible for their effector function,
 - B) having a culture of animal cells expressing on their membranes the GPCR,
 - C) Incubating the cell culture with the phage library obtained In A),
 - D) harvesting the cells after removal of non specifically bond and surface receptor bound phages,
 - E) Releasing the phages internalized in step C) by lysis of cells obtained in D)
 - F) Infecting an *E. coli* culture with the released phages obtained in E) and amplifying the clones previously internalized ,
 - G) Obtaining a phage library enriched in internalizing chemokines ligands,
 - H) Assaying the agonist or antagonist property of the chemokine variants versus the native one.
2. (Withdrawn) The method according to claim 1 wherein the chemokine is RANTES.
3. (Withdrawn) The method according to claim 1 wherein the GPCR expressed within the membrane of animal cells is CCR5.

4. (Withdrawn) The method according to claim 1 wherein the animal cells are human cells.

5. (Withdrawn) The method according to claim 2 wherein the phage library of RANTES variants is obtained using a method comprising the following steps:

- a. Obtaining a DNA sequence coding for human RANTES resulting from the amplification of cDNA prepared from activated PBMCs,
- b. Performing a PCR mutagenesis of the 5' portion of the DNA sequence of RANTES using a specific downstream primer and a degenerate upstream primer containing recognition sites for restriction enzymes in order to insert the PCR amplification products into the phage display vector,
- c. Inserting the purified PCR products into a phage display vector,
- d. Production of the phage library by introducing the vector containing the purified PCR products into an *E. coli* culture.

6. (Withdrawn) The method according to claim 2 wherein anti-HIV activity is assayed.

7. (Withdrawn) A method for the design and/or the selection of chemokines having agonist or antagonist property towards a GPCR of animal cells comprising the following steps:

- i. obtaining a phage displayed library expressing on their surface said chemokine mutated within the domain responsible for their effector function,
- ii. having a culture of animal cells expressing on their membranes the GPCR,
- iii. Incubating the cell culture with the phage library obtained in A),
- iv. Eliminating the non specifically bond phages from the cells, by a process keeping the specifically bound phages on the said receptor

- v. Incubating the cells obtained in D) with an *E. coli* culture and amplifying the clones being infected by the phages bound to the said receptor on animal cells,
- vi. Obtaining a phage library enriched in externally bound phages,
- vii. Assaying the agonist or antagonist property of the chemokine variants versus the native chemokine.

8. (Withdrawn) The method according to claim 7 wherein the chemokine is RANTES.

9. (Withdrawn) The method according to claim 7 wherein the GPCR expressed within the membrane of animal cells is CCR5.

10. (Withdrawn) The method according to claim 7 wherein the animal cells are human cells.

11. (Withdrawn) The method according to claim 8 wherein the phage library of RANTES variants is obtained using a method comprising the following steps:

- a. Obtaining a DNA sequence coding for human RANTES resulting from the amplification of cDNA prepared from activated PBMCs,
- b. Performing a PCR mutagenesis of the 5'portion of the DNA sequence of RANTES using a specific downstream primer and a degenerate upstream primer containing recognition sites for restriction enzymes in order to insert the PCR amplification products into the phage display vector,
- c. Inserting the purified PCR products into a phage display vector,
- d. Production of the phage library by introducing the vector containing the purified PCR products into an *E. coli* culture.

12. (Withdrawn) The method according to claim 8 wherein anti-HIV activity is assayed.

13. (Currently Amended) A compound ~~obtainable by a method according to anyone of claims 1 to 12 of~~ comprising the following formula: *XaaSP#Xaa&&& Xaa, Xaa, Xaa (SEQ ID NO:40) in which

- a. * Xaa at position 1 is L or an aromatic residue,
- b. # Xaa at position 4 is L, M or V
- c. & Xaa at position 8-10 is S, P, T or A.

14. (Currently Amended) The compound according to claim 13 having one of the following formulae :

LSPVSSQSSA	(SEQ ID NO: 1) (P ₁)
FSPLSSQSSA	(SEQ ID NO: 2) (P ₂)
LSPMSSQSPA	(SEQ ID NO: 3)
WSPLSSQSPA	(SEQ ID NO: 4)
WSPLSSQSSP	(SEQ ID NO: 5)
LSPQSSLSSS	(SEQ ID NO: 6)
ASSGSSQSTS	(SEQ ID NO: 7)
ISAGSSQSTS	(SEQ ID NO: 8)
RSPMSSQSSP	(SEQ ID NO: 9)
YSPSSSLAPA	(SEQ ID NO: 10)
MSPLSSQASA	(SEQ ID NO: 11)
ASPMSSQSSS	(SEQ ID NO: 12)
QSPLSSQAST	(SEQ ID NO: 13)

QSPLSSTASS	(SEQ ID NO: 14)
LSPLSSQSAA	(SEQ ID NO: 15)
GSSSSSQTPA	(SEQ ID NO: 16)
YSPLSSQSSP	(SEQ ID NO: 17)
FSSVSSQSSS,	(SEQ ID NO: 18)
VSTLSSPAST,	(SEQ ID NO: 30)
ASSFSSRAPP,	(SEQ ID NO: 31)
QSSASSSSSA	(SEQ ID NO: 32)
QSPGSSWSAA,	(SEQ ID NO: 33)
QSPPSSWSSS,	(SEQ ID NO: 34)
QSPLSSFTSS,	(SEQ ID NO: 35)
LSPQSSLSSS,	(SEQ ID NO: 6)
ASPQSSLPAA,	(SEQ ID NO: 36)
(1) LSPVSSQSSA	(SEQ ID NO: 1)

15. (Withdrawn) The compound according to claim 13 having the formula:
FSPLSSQSSA(SEQ ID N): 2-RANTES(10-68).

16. (Withdrawn) The compound according to claim 13 having the formula:
LSPVSSQSSA-RANTES (10-68).

17. (Currently Amended) A pharmaceutical composition which comprises of a compound having the formula: *XaaSP#Xaa&&& Xaa, Xaa, Xaa (SEQ ID NO:40) in which

- * Xaa at position 1 is L or an aromatic residue,
- # Xaa at position 4 is L, M or V
- & Xaa at position 8-10 is S, P, T or A.

or a pharmaceutical salt thereof, in a mixture with one or more pharmaceutically acceptable excipient.

18. (Withdrawn) The composition of claim 17 in which the compound have the formula: LSPVSSQSSA(SEQ ID NO: 1)- RANTES(10-68).

19. (Withdrawn) The composition of claim 17 in which the compound have the formula: FSPLSSQSSA (SEQ ID NO:2) -RANTES-(10-68).

20. (Withdrawn) A method for preventing and/or inhibiting HIV infection in humans comprising a step of treatment with a composition of claim 18.

21. (Withdrawn) A method for preventing and/or inhibiting HIV infection in humans comprising a step of treatment with a composition of claim 19.

22. (Withdrawn)A method for preventing and/or curing inflammatory or malignant diseases in humans comprising a step of treatment with a composition of claim 13 or 14.

Please add the following new claims:

23. (New) A compound comprising one of the following formulae :

LSPQSSLSSS (SEQ ID NO: 6),
ASSGSSQSTS (SEQ ID NO: 7),
ISAGSSQSTS (SEQ ID NO: 8),
RSPMSSQSSP (SEQ ID NO: 9),
YSPSSLAPA (SEQ ID NO: 10),

MSPLSSQASA (SEQ ID NO: 11),
ASPMSSQSSS (SEQ ID NO: 12),
QSPLSSQAST (SEQ ID NO: 13),
QSPLSSTASS (SEQ ID NO: 14),
GSSSSSQTPA (SEQ ID NO: 16),
FSSVSSQSSS, (SEQ ID NO: 18),
VSTLSSPAST, (SEQ ID NO: 30),
ASSFSSRAPP, (SEQ ID NO: 31),
QSSASSSSSA (SEQ ID NO: 32),
QSPGSSWSAA, (SEQ ID NO: 33),
QSPPSSWSSS, (SEQ ID NO: 34),
QSPLSSFTSS, (SEQ ID NO: 35) and
AS PQSSLPA A, (SEQ ID NO: 36).

24. (New) A compound consisting essentially of one of the following formulae :

LSPQSSLSSS (SEQ ID NO: 6),
ASSGSSQSTS (SEQ ID NO: 7),
ISAGSSQSTS (SEQ ID NO: 8),
RSPMSSQSSP (SEQ ID NO: 9),
YSPSSLAPA (SEQ ID NO: 10),
MSPLSSQASA (SEQ ID NO: 11),
ASPMSSQSSS (SEQ ID NO: 12),
QSPLSSQAST (SEQ ID NO: 13),
QSPLSSTASS (SEQ ID NO: 14),
GSSSSSQTPA (SEQ ID NO: 16),
FSSVSSQSSS, (SEQ ID NO: 18),

VSTLSSPAST, (SEQ ID NO: 30),
ASSFSSRAPP, (SEQ ID NO: 31),
QSSASSSSA (SEQ ID NO: 32),
QSPGSSWSAA, (SEQ ID NO: 33),
QSPPSSWSSS, (SEQ ID NO: 34),
QSPLSSFTSS, (SEQ ID NO: 35) and
AS PQSSLPA A, (SEQ ID NO: 36).

25. (New) A pharmaceutical composition which comprises one of the following formulae:

LSPQSSLSSS (SEQ ID NO: 6),
ASSGSSQSTS (SEQ ID NO: 7),
ISAGSSQSTS (SEQ ID NO: 8),
RSPMSSQSSP (SEQ ID NO: 9),
YSPSSSLAPA (SEQ ID NO: 10),
MSPLSSQASA (SEQ ID NO: 11),
ASPMSSQSSS (SEQ ID NO: 12),
QSPLSSQAST (SEQ ID NO: 13),
QSPLSSTASS (SEQ ID NO: 14),
GSSSSSQTPA (SEQ ID NO: 16),
FSSVSSQSSS, (SEQ ID NO: 18),
VSTLSSPAST, (SEQ ID NO: 30),
ASSFSSRAPP, (SEQ ID NO: 31),
QSSASSSSA (SEQ ID NO: 32),
QSPGSSWSAA, (SEQ ID NO: 33),
QSPPSSWSSS, (SEQ ID NO: 34),
QSPLSSFTSS, (SEQ ID NO: 35) and
AS PQSSLPA A, (SEQ ID NO: 36).

or a pharmaceutical salt thereof, in a mixture with one or more pharmaceutically acceptable excipient.

26. (New) A pharmaceutical composition consisting essentially of one of the following formulae:

LSPQSSLSSS	(SEQ ID NO: 6),
ASSGSSQSTS	(SEQ ID NO: 7),
ISAGSSQSTS	(SEQ ID NO: 8),
RSPMSSQSSP	(SEQ ID NO: 9),
YSPSSSLAPA	(SEQ ID NO: 10),
MSPLSSQASA	(SEQ ID NO: 11),
ASPMSSQSSS	(SEQ ID NO: 12),
QSPLSSQAST	(SEQ ID NO: 13),
QSPLSSTASS	(SEQ ID NO: 14),
GSSSSSQTPA	(SEQ ID NO: 16),
FSSVSSQSSS,	(SEQ ID NO: 18),
VSTLSSPAST,	(SEQ ID NO: 30),
ASSFSSRAPP,	(SEQ ID NO: 31),
QSSASSSSA	(SEQ ID NO: 32),
QSPGSSWSAA	(SEQ ID NO: 33),
QSPPSSWSSS,	(SEQ ID NO: 34),
QSPLSSFTSS,	(SEQ ID NO: 35) and
ASPQSSLPA,	(SEQ ID NO: 36).

or a pharmaceutical salt thereof, in a mixture with one or more pharmaceutically acceptable excipient.